Rejections Under 35 U.S.C. §112, First Paragraph

Claims 46-86 and 17-18 are rejected as allegedly containing "no clear written description in the specification about SEQ.ID.NOS which are recited." Applicant respectfully disagrees. The SEQ ID NOS referenced in the claims are SEQ ID NOS:1-8, 10, and 12-15. The referenced sequences and their assigned SEQ ID NOS are pictured in the drawings, specifically in Figures 19-28. Thus, applicant submits that the SEQ ID NOS satisfy the requirement for a clear written description.

The Examiner states that the use of the term "comprising" in a claim requires information regarding "what else the sequence contain besides the one is in the sequence listing [sic]." Applicant is unaware of any requirement that the term "comprising" be limited as the Examiner suggests. If the Examiner's concern is that the claims encompass an entire chromosome from a wild type cell, Applicant points out that each claim using the term "comprising" (claims 17, 47-51, 53-57, 59-63, 65-69, 71-75, 77-81, and 83-86) ultimately depends from a claim that is drawn to "an isolated nucleic acid molecule" (emphasis added). Therefore, the claims do not encompass an entire chromosome from a wild-type cell and the term "comprising" is appropriately used in the claims. The Examiner asked whether the Applicant has cDNA. The Applicant does not understand the Examiner's question. SspB, sspC, sspD, and sspA are bacterial genes. Thus, they were cloned and sequenced without producing cDNA. Applicant respectfully requests that the Examiner clarify her inquiry. If the Examiner is concerned that the disclosed sequences include intron sequences, the concern is unwarranted. As bacterial genes, the sspB, sspC, sspD, and sspA genes do not include introns.

The Examiner also asserts that claim 17 "does not describe the usefulness of uptake of a bacterial cell by an epithelial cell and also administering this cell to a mammal would lead to what function?" Applicant respectfully submits that the specification provides ample description of the use of the claimed invention. For example, the specification states that

> [a]n Ssp...can be used to translocate a second molecule, e.g., a polypeptide, into the cytoplasm of a cell. This approach can be useful for the induction or priming of cytotoxic lymphocytes (CTL) directed against the second molecule. An

> Ssp...can be used to introduce a second molecule into the cell cytoplasm for the purpose of drug delivery.

Thus, the specification fully discloses a specific, substantial and credible utility for the claimed method. Applicant does not believe that it is necessary for the claim itself to recite the usefulness of the method. The Examiner argued that [s]ince there is no clear description of the SEQ ID NO 1 and 2 this method need to written more clearly with specific use." However, as explained above, the specification does have clear description of SEQ ID NO:1 and SEQ ID NO:2. Thus, it is Applicant's position that claim 17 meets the written description requirement.

In view of the above arguments, applicant requests that the § 112, first paragraph rejections be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 46, 52, 58, 64, 70, 76, and 82 are rejected as allegedly vague and indefinite for using the language "hybridizes under conditions of hybridization in 50% formamide at 42° (sic) washing in 0.1X SSC at 65° (sic)." Applicant respectfully disagrees with the allegation. First, the Examiner asks "[w]hat are these hybridizing conditions..." Applicant submits that the hybridizing conditions are well-known to those in the art and are also disclosed in the specification at page 5, line 26-35. Moreover, the hybridization conditions are recited in the claims themselves. The next question asked by the Examiner is "which part of the sequence hybridizes to what?" The claim states a clear test for determining the metes and bounds of the invention. If a nucleic acid molecule hybridizes under the recited conditions to the specified nucleic acid molecule, the nucleic acid molecule is encompassed by the claim. The Examiner also asks "What are these sequences?" Applicant does not understand the question. The claims encompass nucleic acid molecules that hybridize under highly stringent conditions to the sequences identified by their SEQ ID NOS. There is no need for the claims to recite the sequences of the claimed molecules as well. Finally, Applicant does not understand the relevance of the Examiner's question as to whether the hybridization conditions are the "actual conditions used in the specification." As discussed above, they are, indeed, hybridization conditions disclosed in the invention.

The Examiner asked for clarification of the term "SSC." SSC is a solution that has been well-known in the art for many years and is frequently used in claims involving nucleic acid hybridization conditions. In fact, the term is so common that it has ceased to be an abbreviation and has become a term of art much as "DNA" and "cDNA" are terms of art. In view of the general knowledge in the art of the term, Applicant submits that one in the art would know what SSC is and it is not necessary to amend the claims to give its composition. In view of the forgoing, Applicant requests that the § 112, second paragraph rejections be withdrawn.

Rejections Under 35 U.S.C. § 102 (e)

Claims 46-86 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by WO 95/02048 (the '048 application). It does not appear that the '048 application is citable under 35 U.S.C. §102(e), which specifies that "[a] person is entitled to a patent unless – (e) the invention was described in patent granted ...on an international application before the invention thereof by the applicant for the patent." Applicant points out that the '048 application is a patent application, not a granted patent. Therefore, the rejection under 35 U.S.C. § 102(e) is improper. Applicant assumes that the Examiner intended to reject the present application under 35 U.S.C. § 102(a). Applicant respectfully requests that the Examiner clarify the rejection. The following response to the assumed rejection is provided below.

In her rejection of the pending claims as anticipated by the '048 application, the Examiner asserts that the claims "are directed to an isolated nucleic acid molecules (sic) encoding a Salmonella secreted protein." Applicant submits that this is an imprecise characterization of the claim. Claims 46-86 are drawn to SspB, SspC, SspD, and SspA and nucleic acid molecules encoding these proteins. The '048 application does not appear to disclose specific nucleotide or amino acid sequences related to any of these genes. Thus, it does not appear that the '048 application can anticipate any of claims 46-86.

The Examiner stated that the '048 application discloses that secretion of Salmonella protein is dependent on PrgH. The present claims are not drawn to PrgH, and Applicant cannot understand the relevance of the Examiner's remarks concerning PrgH.

In view of the above arguments, applicant requests that the assumed § 102 (a) rejection in view of WO 95/02098 be withdrawn.

Rejections Under 35 U.S.C. § 102 (a)

Claims 46-86 and 17-18 are rejected as allegedly anticipated by Hueck et al. (Molecular Microbiology 18: 579-490, 1995; "Hueck"), Kaniga et al. (Journal of Bacteriology 177: 3965-3971, 1995; "Kaniga"), and Hermant et al. (Molecular Microbiology 17: 781-789, 1995; "Hermant"). Applicant respectfully disagrees.

The present application has an filing date of May 14, 1998. It is a U.S. National Phase application filed under 35 U.S.C. § 371 of PCT/US96/18504, filed November 14, 1996. The PCT application claims priority from U.S. Patent Application No. 60/006,733, filed November 14, 1995.

Hueck is not prior art under 102(a) because it was published after the priority date of the present application. As evidence of this, applicant submits a date stamped copy of the Hueck reference from Northeastern University, Boston, MA (Exhibit A). The date stamp indicates that the journal was received by Northeastern University on December 6, 1995. Applicant filed the priority application with the U.S. Patent and Trademark Office on November 14, 1995, before the Hueck reference was made available to the public. Therefore, Hueck does not qualify as prior art to the present application.

Kaniga discloses the amino acid sequences of SipB and SipC. Unlike the present application, Kaniga does not disclose any nucleic acid sequences. Furthermore, Kaniga does not disclose any nucleic acid sequences or amino acid sequences for SspD or SspA. The Examiner fails to explain how Kaniga can anticipate SspD or SspA. Nor does the Examiner explain how disclosure of the amino acid sequences of SipB and Sip C can anticipate the nucleic acid sequences of SspB and SspC. The Examiner has failed to establish why any of the claims related to SspA or SspD amino acids or nucleic acids and claims related to SspB and SspC nucleic acids are anticipated by Kaniga.

Applicant does not understand the relevance of the Examiner's statement that "Salmonella typhimurium is an wild type bacteria and hence contain SspB, SspC, SspD and SspA genes." Applicant is not claiming Salmonella typhimurium. Applicant is claiming specific, isolated nucleic acid sequences.

The earliest date the Kaniga reference was made available to the public was July 8, 1995. As evidence of this date, Applicant submits a letter from Linda Illig, the Director of Journals at the American Society for Microbiology, who states that the issue of the Journal of Bacteriology that contained the Kaniga reference was first made available to the public on July 8, 1995 . (Exhibit B). As demonstrated in the accompanying Declaration under 37 C.F.R. § 1.131 of Dr. Samuel Miller (Exhibit C), Dr. Miller had cloned and obtained sequence information for SspB, SspC, SspD, and SspA prior to July 8, 1995.

Hermant discloses the amino acid sequences of SipA, SipB, SipC, SipD, and SipE. Unlike the present application, Hermant does not disclose any nucleic acid sequences. The Examiner does not explain how disclosure of the amino acid sequences of SipA, SipB, Sip C, SipD, and SipE can anticipate the nucleic acid sequences of SspB, SspC, SspD, or SspA.

Hermant was made available to the public on October 3, 1995. As evidence of this, Applicant has obtained a date stamped copy of the Hermant reference from the Massachusetts Institute of Technology (MIT) in Cambridge, MA (Exhibit D). The date stamp indicates that the journal was received by MIT on October 3, 1995. As demonstrated in the accompanying Declaration Under 37 C.F.R. 1.131 of Dr. Samuel Miller (Exhibit C), Dr. Miller had cloned and obtained sequence information for SspB, SspC, SspD, and SspA prior to July 8, 1995. In view of the Declaration, applicant submits that Hermant is removed as prior art under §102 (a).

In the Response filed on April 14, 2000, Applicant submitted a Declaration under 37 C.F.R. 1.131 stating that the manuscript for Hueck was submitted for publication before the critical date of July 8, 1995. Applicant disagrees with the Examiner's judgment that the manuscript cannot serve as evidence of reduction to practice. However, to expedite prosecution, Applicant has submitted the evidence of reduction to practice discussed above and reserves the right to further address the Examiner's judgment regarding the submitted manuscript.

In view of the above, Applicant requests that the § 102(a) rejections be withdrawn.

CONCLUSION

Applicant submits that all of the claims are now in condition for allowance, which action is requested. Filed herewith is a check in payment of the excess claims fees required by the above amendments and Petition for Automatic Extension with the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 00786-292002.

Respectfully submitted,

Date: 16 FEBRUARY 2001

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APPENDIX

17. A method of inducing uptake of a bacterial cell by an epithelial cell in a mammal, comprising increasing expression of the nucleic acid molecule of claim 46 or 52 in said bacterial cell and administering said bacterial cell to said mammal.

18. The method of claim 17, wherein said bacterial cell is a *Salmonella* cell.

46. An isolated nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:1.

47. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 5.

48. The isolated nucleic acid molecule of claim 47 comprising the nucleotide sequence of SEQ ID NO: 1.

49. A vector comprising the isolated nucleic acid molecule of any of claims 46, 47, or 48.

50. A host cell comprising the isolated nucleic acid molecule of any of claims 46, 47, or 48.

51. A host cell comprising the vector of claim 49.

52. An isolated nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:2.

53. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:6.

54. The isolated nucleic acid molecule of claim 52 comprising the nucleotide sequence of SEQ ID NO: 2.

55. A vector comprising the isolated nucleic acid molecule of any of claims 52, 53, or 54.

56. A host cell comprising the isolated nucleic acid molecule of any of claims 52, 53, or 54.

57. A host cell comprising the vector of claim 55.

58. An isolated nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:3.

59. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:7.

60. The isolated nucleic acid molecule of claim 59 comprising the nucleotide sequence of SEQ ID NO: 3.

61. A vector comprising the isolated nucleic acid molecule of any of claims 58, 59, or 60.

62. A host cell comprising the isolated nucleic acid molecule of any of claims 58, 59, or 60.

63. A host cell comprising the vector of claim 61.

64. An isolated nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:4.

65. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:8.

66. The isolated nucleic acid molecule of claim 65 comprising the nucleotide sequence of SEQ ID NO:4.

67. A vector comprising the isolated nucleic acid molecule of any of claims 64, 65, or 66.

68. A host cell comprising the isolated nucleic acid molecule of any of claims 64, 65, or 66.

69. A host cell comprising the vector of claim 67.

70. An isolated nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:13.

71. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 14.

72. The isolated nucleic acid molecule of claim 71 comprising the nucleotide sequence of SEQ ID NO: 13.

73. A vector comprising the isolated nucleic acid molecule of any of claims 70, 71, or 72.

74. A host cell comprising the isolated nucleic acid molecule of any of claims 70, 71, or 72.

75. A host cell comprising the vector of claim 73.

76. An isolated nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42°C and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:10.

77. An isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 12.

78. The isolated nucleic acid molecule of claim 77 comprising the nucleotide sequence of SEQ ID NO: 10.

79. A vector comprising the isolated nucleic acid molecule of any of claims 76, 77, or 78.

80. A host cell comprising the isolated nucleic acid molecule of any of claims 76, 77, or 78.

81. A host cell comprising the vector of claim 79.

82. An isolated nucleic acid molecule which hybridizes under conditions of hybridization in 50% formamide at 42oC and washing in 0.1 X SSC at 65°C to a nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO:15.

83. The isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 15.

84. A vector comprising the isolated nucleic acid molecule of any of claims 82 or 83.

85. A host cell comprising the isolated nucleic isolated acid molecule of any of claims 82 or 83.

86. A host cell comprising the vector of claim 84.